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```
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      3
         May 12
                 EXTEND option available in structure searching
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         May 12
                 Polymer links for the POLYLINK command completed in REGISTRY
NEWS
         May 27
                 New UPM (Update Code Maximum) field for more efficient patent
                 SDIs in CAplus
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                 CAplus super roles and document types searchable in REGISTRY
      6
         May 27
NEWS
      7
         Jun 28
                 Additional enzyme-catalyzed reactions added to CASREACT
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      8
         Jun 28
                 ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG,
                 and WATER from CSA now available on STN(R)
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      9
         Jul 12
                 BEILSTEIN enhanced with new display and select options,
                 resulting in a closer connection to BABS
NEWS 10
         Jul 30
                 BEILSTEIN on STN workshop to be held August 24 in conjunction
                 with the 228th ACS National Meeting
NEWS 11
         AUG 02
                 IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                 fields
NEWS 12
         AUG 02
                 CAplus and CA patent records enhanced with European and Japan
                 Patent Office Classifications
NEWS 13
         AUG 02
                 STN User Update to be held August 22 in conjunction with the
                 228th ACS National Meeting
NEWS 14
         AUG 02
                 The Analysis Edition of STN Express with Discover!
                 (Version 7.01 for Windows) now available
NEWS 15
         AUG 04
                 Pricing for the Save Answers for SciFinder Wizard within
                 STN Express with Discover! will change September 1, 2004
              JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
NEWS EXPRESS
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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              General Internet Information
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FILE 'HOME' ENTERED AT 13:04:37 ON 17 AUG 2004

=> file medline biosis embase caplus

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FULL ESTIMATED COST

ENTRY 0.21 SESSION 0.21

FILE 'MEDLINE' ENTERED AT 13:04:53 ON 17 AUG 2004

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=> s luo ying/au

219 LUO YING/AU

=> s mancebo helena/au

6 MANCEBO HELENA/AU

=> s syk (s) ubp (s) protein

3 SYK (S) UBP (S) PROTEIN L₃

=> dup rem 13

PROCESSING COMPLETED FOR L3

3 DUP REM L3 (0 DUPLICATES REMOVED)

=> d l4 total ibib kwic

ANSWER 1 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

2004:237339 BIOSIS PREV200400237391

TITLE:

SYK-UBP proteins,

AUTHOR (S):

compositions and methods of use. Luo, Ying [Inventor, Reprint Author]; Mancebo, Helena

[Inventor]

CORPORATE SOURCE:

San Bruno, CA, USA

ASSIGNEE: Rigel Pharmaceuticals, Inc.

PATENT INFORMATION: US 6709839 March 23, 2004

SOURCE:

Official Gazette of the United States Patent and Trademark

Office Patents, (Mar 23 2004) Vol. 1280, No. 4. http://www.uspto.gov/web/menu/patdata.html. e-file.

ISSN: 0098-1133 (ISSN print).

DOCUMENT TYPE:

Patent

LANGUAGE:

English

ENTRY DATE:

Entered STN: 28 Apr 2004

Last Updated on STN: 28 Apr 2004

TT SYK-UBP proteins, compositions and methods

of use.

IT Major Concepts

Methods and Techniques; Pharmacology

TT Diseases

disease: disease-miscellaneous

Disease (MeSH)

Chemicals & Biochemicals IT

SYK-UBP proteins: diagnostic-drug;

nucleic acids; polypeptides

ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN T.4

ACCESSION NUMBER:

2003:376376 CAPLUS

DOCUMENT NUMBER:

138:364551

TITLE:

Novel human SYK kinase-associated cell cycle protein

sequence and modulation of leukocyte activation,

compositions and methods of use

INVENTOR(S):

Wong, Brian; Fu, Chong Alan; Mancebo, Helena; Zhou,

Xiulan X. Z.

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 88 pp., Cont.-in-part of U.S.

Ser. No. 39,761.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND APPLICATION NO. PATENT NO. DATE DATE _____ ---------_____ 20030515 US 2002-112674 US 2003092605 US 2003036107 A1 20020329 A1 20030220 US 2001-39761 20011019 P 20010329 PRIORITY APPLN. INFO.: US 2001-280698P US 2001-39761 A2 20011019 US 1999-404967 A 19990924 WO 2000-US26338 W 20000925

The present invention provides compns. and methods for modulating AB leukocyte activation. The invention provides protein and cDNA sequences for novel human SYK kinase-associated cell cycle proteins SYK-UBP. Nucleic acids encoding proteins and proteins so encoded which are capable of modulating leukocyte

activation are provided. Compns. and methods for the treatment of disorders related to leukocyte dysfunction or dysregulation are also provided. Prophylactics and methods for the prevention of such disorders are also provided. Also provided are compns. and methods for diagnostic and prognostic determination of such disorders. Further provided are assays

for

the identification of bioactive agents capable of modulating leukocyte activation.

IT331009-92-8D, Protein SYK-UBP (human isoform

1), Subfragments are claimed

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence; novel human SYK kinase-associated cell cycle protein sequence and modulation of leukocyte activation, compns. and methods of use)

ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:228922 CAPLUS

DOCUMENT NUMBER:

134:247997

TITLE:

Novel SYK kinase-associated cell cycle

proteins SYK-UBPs,

compositions and methods of use

INVENTOR(S):

Luo, Ying; Mancebo, Helena

PATENT ASSIGNEE(S):

Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				
WO 2001021654	A2	20010329	WO 2000-US26338	20000925
WO 2001021654	A3	20020307		
ער און אין און	TTO			

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

```
PT, SE
     US 6709839
                           В1
                                 20040323
                                             US 1999-404967
                                                                    19990924
     AU 2000078328
                          Α5
                                 20010424
                                            AU 2000-78328
                                                                    20000925
     EP 1218505
                          A2
                                20020703 EP 2000-968406
                                                                    20000925
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         R:
             IE, FI, CY
     JP 2003512820
                          T2
                                20030408
                                             JP 2001-525227
                                                                    20000925
     US 2003036107
                          Αl
                                20030220
                                             US 2001-39761
                                                                    20011019
PRIORITY APPLN. INFO.:
                                             US 1999-404967
                                                                A2 19990924
                                             WO 2000-US26338
                                                                W 20000925
                                             US 2001-280698P
                                                                P 20010329
     Novel SYK kinase-associated cell cycle proteins
TI
     SYK-UBPs, compositions and methods of use
     The invention provides protein and cDNA sequences for novel
AB
     human SYK kinase-associated cell cycle proteins
     SYK-UBPs, which have an effect on or are related to the
     cell cycle. Also provided herein are vectors and host cells comprising
     those nucleic acid sequences, chimeric polypeptide mols. comprising the
     polypeptides of the present invention fused to heterologous polypeptide
     sequences, antibodies which bind to the polypeptides of the present
     invention and to methods for producing the polypeptides of the present
     invention. Further provided by the present invention are methods for
     identifying novel compns. which mediate cell cycle bioactivity, and the
     use of such compns. in diagnosis and treatment of disease.
IT
     Proteins, specific or class
     RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU
     (Biological study, unclassified); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (SYK-UBP, of human; novel SYK
        kinase-associated cell cycle proteins SYK-UBPs
        , compns. and methods of use)
IT
     cDNA sequences
        (for protein SYK-UBP, of human; novel
        SYK kinase-associated cell cycle proteins SYK-
        UBPs, compns. and methods of use)
IT
     Gene, animal
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for protein SYK-UBP, of human; novel
        SYK kinase-associated cell cycle proteins SYK-
        UBPs, compns. and methods of use)
ΙT
     Diagnosis
        (mol.; novel SYK kinase-associated cell cycle proteins
        SYK-UBPs, compns. and methods of use)
IT
     Antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (monoclonal, to protein SYK-UBP; novel
        SYK kinase-associated cell cycle proteins SYK-
        UBPs, compns. and methods of use)
IT
     Cell cycle
     Drug screening
     Gene therapy
     Molecular cloning
     Nucleic acid hybridization
        (novel SYK kinase-associated cell cycle proteins
        SYK-UBPs, compns. and methods of use)
TT
     Primers (nucleic acid)
     Probes (nucleic acid)
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (novel SYK kinase-associated cell cycle proteins
        SYK-UBPs, compns. and methods of use)
IT
     Protein sequences
        (of protein SYK-UBP, of human; novel
        SYK kinase-associated cell cycle proteins SYK-
```

```
UBPs, compns. and methods of use)
IT
     Antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (to protein SYK-UBP; novel SYK
        kinase-associated cell cycle proteins SYK-UBPs
        , compns. and methods of use)
IT
     Protein motifs
        (ubiquitin-associated binding domain in protein SYK-
        UBP; novel SYK kinase-associated cell cycle
        proteins SYK-UBPs, compns. and methods of
        use)
IT
     Protein motifs
        (ubiquitin-specific protease domain in protein SYK-
        UBP; novel SYK kinase-associated cell cycle
        proteins SYK-UBPs, compns. and methods of
        use)
IT
     331009-92-8P, Protein SYK-UBP (human isoform
          331009-93-9P, Protein SYK-UBP (human
     1)
     isoform 2)
     RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU
     (Biological study, unclassified); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (amino acid sequence; novel SYK kinase-associated cell cycle
        proteins SYK-UBPs, compns. and methods of
        use)
IT
     60267-61-0, Ubiquitin
                             138674-26-7, SYK kinase
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (cell cycle protein SYK-UBP interacting
        with; novel SYK kinase-associated cell cycle proteins
        SYK-UBPs, compns. and methods of use)
IT
     331009-94-0
                   331009-95-1
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nucleotide sequence; novel SYK kinase-associated cell cycle
        proteins SYK-UBPs, compns. and methods of
        use)
IT
     331011-23-5
     RL: PRP (Properties)
        (unclaimed protein sequence; novel SYK
        kinase-associated cell cycle proteins SYK-UBPs
        , compns. and methods of use)
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L Number	Hits	Search Text	DB	Time stamp
1	27	luo-ying.in.	USPAT;	2004/08/17 11:55
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
2	4	mancebo-helena.in.	USPAT;	2004/08/17 11:56
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
3	3	syk-ubp same protein	USPAT;	2004/08/17 11:56
			US-PGPUB;	
			EPO; JPO;	
1			DERWENT	

10088960 Results

SEQ ID NO: 2

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                Query
        Score Match Length DB ID
                                                           Description
  No.
                                                            Human SYK kinase b
    1
         5473 100.0
                      1055 22 AAB74491
                                                            A human ubiquitin
     2
          5460
                99.7
                        1055 22 AAB31546
                        1055 22 AAB31552
                                                            A human ubiquitin
     3
          5460
                99.7
                        1075 22 AAB74492
                                                            Human SYK kinase b
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                99.6
                       1087 22 AAB31550
1087 22 AAB31556
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          5430
                99.2
                                                            A human ubiquitin
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          5430
                 99.2
                                                            A human ubiquitin
                                                            Human SYK kinase b
          4308
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     8
         3741
                 68.3
                         720 20 AAY45343
                                                            Human secreted pro
                             21
                                 AAG03009
                                                            Human secreted pro
     9
          344
                 6.3
                         71
                        1264 14 AAR36730
                                                            Ubiquitin-specific
    10
        318.5
                 5.8
    11
           224
                 4.1
                        2547 19 AAW81511
                                                            Drosophila fat fac
                        912 22 AAB75607
2954 20 AAY01632
           215
                                                            Human cancer assoc
    12
                 3.9
    13
        214.5
                 3.9
                                                            Amino acid sequenc
                        1517 21 AAG38482
                                                            Arabidopsis thalia
        213.5
                 3.9
    14
                                                            Arabidopsis thalia
    15
        213.5
                  3.9
                        1543 21 AAG38481
RESULT
AAY45343
ID
    AAY45343 standard; Protein; 720 AA.
XX
AC
    AAY45343:
XX
     23-NOV-1999 (first entry)
DT
XX
     Human secreted protein fragment encoded from gene 23.
DE
XX
     Secreted protein; human; gene therapy; diagnosis; treatment; cancer;
KW
     protein therapy; tumor; neurodegenerative disorder; blood disorder; AIDS;
KW
KW
     developmental abnormality; leukemia; immune system; autoimmune disease;
     hepatic disease; renal disease; inflammation; allergy; schizophrenia;
KW
     Alzheimer's disease; cognitive disorder; arthritis; infection; psoriasis;
KW
KW
     transplant rejection; diabetes; asthma; sepsis; acne; metabolic disorder;
KW
     cardiovascular disorder; food additive; preservative.
XX
os
    Homo sapiens.
XX
PN
     WO9946289-A1.
XX
PD
     16-SEP-1999.
XX
PF
     11-MAR-1999;
                    99WO-US05721.
XX
PR
     12-MAR-1998:
                    98US-0077686.
PR
     12-MAR-1998;
                    98US-0077687.
    12-MAR-1998;
PR
                    98US-0077696.
PR
     12-MAR-1998;
                    98US-0077714.
XX
PΑ
     (HUMA-) HUMAN GENOME SCI INC.
XX
     Ruben SM, Ferrie AM, Rosen CA, Florence C, Young PE, Yu G, Ni J;
PΤ
XX
DR
     WPI: 1999-551363/46.
DR
     N-PSDB; AAZ27255.
XX
     New isolated human genes, useful for diagnosis and treatment of, e.g.
PT
PT
XX
PS
     Disclosure; 214-216; 306pp; English.
XX
CC
     This invention describes novel human genes and the secreted proteins
     they encode. The polynucleotides and their corresponding secreted
CC
     polypeptides are useful for preventing, treating or ameliorating medical
CC
```

```
conditions e.g. by protein or gene therapy. Also pathological conditions
    can be diagnosed by determining the amount of the new polypeptides in a
CC
CC
    sample or by determining the presence of mutations in the new
    polynucleotides. Specific uses are described for each of the
CC
CC
    polynucleotides of the invention, based on which tissues they are most
    highly expressed in, and include developing products for the diagnosis or
CC
    treatment of cancer, tumors, neurodegenerative disorders, developmental
    abnormalities, blood disorders, leukemias, diseases of the immune system,
CC
    autoimmune diseases, hepatic and renal disease, inflammation, allergies,
CC
    Alzheimer's and cognitive disorders, schizophrenia, arthritis,
    infections, AIDS, transplant rejection, diabetes, asthma, sepsis, acne,
CC
    psoriasis, cardiovascular disorders, and metabolic disorders. The
CC
    polypeptides or polynucleotides can also be used as food additives or
CC
    preservatives. The polypeptides are also useful for identifying their
CC
    binding partners. AAY45290-Y45389 represent human secreted protein
CC
CC
    fragments described in the method of the invention.
XX
SO
    Sequence
             720 AA;
 Query Match
                      68.3%; Score 3741; DB 20; Length 720;
 Best Local Similarity 99.7%; Pred. No. 2.5e-277;
 Matches 718; Conservative
                            0; Mismatches
                                           2; Indels
                                                        0; Gaps
                                                                  0;
     336 CLEAAMIEGEIESLHSENSGKSGQEHWFTGLPPVLTFXLSRFEFNQALGRPEKIHNKLEF 395
        1 cleaamiegeieslhsensgksgqehwftelppvltfelsrfefnqalgrpekihnklef 60
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         Db
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Qу
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     301 lvrdsfggyrnasayclmyindkaqfliqeefnketgqplvgietlppdlrdfveednqr 360
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696 FEKELEEWDAQLAQKALQEKLLASQKLRESETSVTTAQAAGDPEYLEQPSRSDFSKHLKE 755

361 fekeleewdaqlaqkalqekllasqklresetsvttaqaagdpeyleqpsrsdfskhlke 420
756 ETIOIITKASHEHEDKSPETVLOSAIKLEYARLVKLAOEDTPPETDYRLHHVVVYFIONO 815

421 etiqiitkashehedkspetvlqsaikleyarlvklaqedtppetdyrlhhvvvyfiqnq 480 816 APKKIIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEEVNLEEYEEWHQDYRKFR 875

481 apkkiiektllegfgdrnlsfderchnimkvaqaklemikpeevnleeyeewhqdyrkfr 540

996 EMEPHLQEKLTDFLPKLLDCSMEIKSFHEPPKLPSYSTHELCERFARIMLSLSRTPADGR 1055

Qу

Db

0v

Db

Qy

Db

Qу

Db Ov

Db

Ov

Dh

Result No.	Caoro	Query	Length	mp	ID	Description
NO.	Score					Description
1	327.5	6.0	1264	1	US-07-789-915A-6	Sequence 6, Appli
2	327.5	6.0	1264	1	US-08-005-002C-6	Sequence 6, Appli
3	327.5	6.0	1264	1	US-08-487-203A-6	Sequence 6, Appli
4	224	4.1	2547	3	US-09-058-489-35	Sequence 35, Appl
5	210	3.8	2555	3	US-09-058-489-36	Sequence 36, Appl
6	186.5	3.4	1786	4	US-08-973-462-8	Sequence 8, Appli
7	178.5	3.3	1164	4	US-08-923-992A-10	Sequence 10, Appl
8	175	3.2	1312	2	US-08-687-080-51	Sequence 51, Appl
9	174	3.2	1312	2	US-08-592-126-148	Sequence 148, App
10	169	3.1	809	1	US-07-789-915A-4	Sequence 4, Appli
11	169	3.1	809	1	US-08-005-002C-4	Sequence 4, Appli
Result		Query				
No.	Score	Match	Length	DB	ID	Description
1	493.5	9.0	1302	2	T23236	hypothetical prote
2	323.5	5.9	1272	2	S60999	ubiquitin-specific
3	313.5	5.7	1108	2	T41188	probable ubiquitin
4	310	5.7	1221	2	T30529	ubiquitin carboxyl
5	287	5.2	1130	2	T23104	hypothetical prote
6	287	5.2	1133	2	T23103	hypothetical prote
7	268.5	4.9	3187	2	JC5837	364K Golgi complex
8	263.5	4.8	1230	2	T19899	hypothetical prote
9	261.5	4.8	1230	2	S53974	hypothetical prote
10	239.5	4.4	1430	2	T21910	hypothetical prote
11	232	4.2	1292	2	T24559	hypothetical prote
Result		Query				
No.	Score	Match	Length	DB	ID	Description
1	3836	70.1	737	4	Q9H9W1	Q9h9w1 homo sapien
2	2741	50.1	523	4	Q9HA22	Q9ha22 homo sapien
3	1895	34.6	757	4	Q9P213	Q9p213 homo sapien
4	301	5.5	1124	10	Q9SF08	Q9sf08 arabidopsis
5	296	5.4	1248	5	Q9VRP1	Q9vrp1 drosophila
6	294	5.4	1126	10	Q9FG10	Q9fg10 arabidopsis
7	293.5	5.4	1116	10	Q9FPT1	Q9fpt1 arabidopsis
8	288.5	5.3	599	10	Q9FU99	Q9fu99 arabidopsis
9	287	5.2	1130	5	045624	045624 caenorhabdi
10	287	5.2	1133	5	045623	045623 caenorhabdi
11	283.5	5.2	1141	3	Q9P3U0	Q9p3u0 schizosacch
12	268.5	4.9	3187	11	•	Q63714 rattus norv
13	264.5	4.8	931	4	Q9HCH8	Q9hch8 homo sapien
14	264.5	4.8	1129	3	Q9UTT1	Q9utt1 schizosacch
15	263.5	4.8	1230	5	Q93371	Q93371 caenorhabdi

SEQ ID NO: 4

Result No.	Score	Query Match	Length	DB	ID	Description
1	5579	100.0	1075	22	AAB74492	Human SYK kinase b
2	5453	97.7	1055	22	AAB74491	Human SYK kinase b
3	5440	97.5	1055	22	AAB31546	A human ubiquitin
4	5440	97.5	1055	22	AAB31552	A human ubiquitin
5	5410	96.9	1087	22	AAB31550	A human ubiquitin
6	5410	96.9	1087	22	AAB31556	A human ubiquitin
7	4308	77.2	834	22	AAB74493	Human SYK kinase b
8	3721	66.7	720	20	AAY45343	Human secreted pro
9	344	6.2	71	21	AAG03009	Human secreted pro
10	318.5	5.7	1264	14	AAR36730	Ubiquitin-specific
11	224	4.0	2547	19	AAW81511	Drosophila fat fac

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RESULT
 AAY45343
 TD
     AAY45343 standard; Protein; 720 AA.
 XX
AC
     AAY45343;
XX
DT
     23-NOV-1999 (first entry)
XX
DE
     Human secreted protein fragment encoded from gene 23.
XX
KW
     Secreted protein; human; gene therapy; diagnosis; treatment; cancer;
KW
     protein therapy; tumor; neurodegenerative disorder; blood disorder; AIDS;
     developmental abnormality; leukemia; immune system; autoimmune disease;
KW
     hepatic disease; renal disease; inflammation; allergy; schizophrenia;
KW
     Alzheimer's disease; cognitive disorder; arthritis; infection; psoriasis;
KW
     transplant rejection; diabetes; asthma; sepsis; acne; metabolic disorder;
KW
     cardiovascular disorder; food additive; preservative.
XX
os
     Homo sapiens.
XX
PN
     WO9946289-A1.
XX
PD
     16-SEP-1999.
XX
PF
     11-MAR-1999;
                    99WO-US05721.
XX
PR
     12-MAR-1998;
                    98US-0077686.
PR
     12-MAR-1998;
                    98US-0077687.
PR
     12-MAR-1998;
                    98US-0077696.
PR
     12-MAR-1998;
                    98US-0077714.
XX
PA
     (HUMA-) HUMAN GENOME SCI INC.
ХX
PΙ
     Ruben SM, Ferrie AM, Rosen CA, Florence C, Young PE, Yu G, Ni J;
XX
DR
     WPI; 1999-551363/46.
DR
     N-PSDB; AAZ27255.
XX
РΤ
     New isolated human genes, useful for diagnosis and treatment of, e.g.
PT
XX
PS
     Disclosure; 214-216; 306pp; English.
xx
     This invention describes novel human genes and the secreted proteins
CC
CC
     they encode. The polynucleotides and their corresponding secreted
     polypeptides are useful for preventing, treating or ameliorating medical
CC
CC
     conditions e.g. by protein or gene therapy. Also pathological conditions
     can be diagnosed by determining the amount of the new polypeptides in a
CC
CC
     sample or by determining the presence of mutations in the new
CC
     polynucleotides. Specific uses are described for each of the
     polynucleotides of the invention, based on which tissues they are most
CC
CC
     highly expressed in, and include developing products for the diagnosis or
     treatment of cancer, tumors, neurodegenerative disorders, developmental
CC
     abnormalities, blood disorders, leukemias, diseases of the immune system,
CC
CC
     autoimmune diseases, hepatic and renal disease, inflammation, allergies,
     Alzheimer's and cognitive disorders, schizophrenia, arthritis,
CC
CC
     infections, AIDS, transplant rejection, diabetes, asthma, sepsis, acne,
     psoriasis, cardiovascular disorders, and metabolic disorders. The
CC
CC
     polypeptides or polynucleotides can also be used as food additives or
CC
     preservatives. The polypeptides are also useful for identifying their
CC
     binding partners. AAY45290-Y45389 represent human secreted protein
CC
     fragments described in the method of the invention.
XX
SQ
     Sequence
               720 AA:
  Query Match
                          66.7%; Score 3721; DB 20; Length 720;
  Best Local Similarity
                         97.0%; Pred. No. 1.9e-278;
  Matches 718; Conservative
                                0; Mismatches
                                                   2; Indels
                                                                20; Gaps
```

1:

```
336 CLEAAMIEGEIESLHSENSGKSGQEHWFTGLPPVLTFXLSRFEFNQALGRPEKIHNKLEF 395
Qγ
       1 cleaamiegeieslhsensgksgqehwftelppvltfelsrfefnqalgrpekihnklef 60
Db
    396 POVLYLDRYMHRNREITRIKREEIKRLKDYLTVLQQRLERYLSYGSGPKRFPLVDVLQYA 455
Qу
       61 pqvlyldrymhrnreitrikreeikrlkdyltvlqqrlerylsygsgpkrfplvdvlqya 120
Db
    456 LEFASSKPVCTSPVDDIDASSPPSGSIPSQTLPSTTEQQGALSSELPSTSPSSVAAISSR 515
Oy
        Db
    121 lefasskpvctspvddidassppsgsipsqtlpstteqqgalsselpstspssvaaissr 180
    516 SVIHKPFTQSRIPPDLPMHPAPRHITEEELSVLESCLHRWRTEIENDTRDLQESISRIHR 575
Qу
        181 svihkpftqsrippdlpmhpaprhiteeelsvlesclhrwrteiendtrdlqesisrihr 240
Db
    576 TIELMYSDKSMIQVPYRLHAVLVHEGQANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEE 635
Qу
        241 tielmysdksmiqvpyrlhavlvhegqanaghywayifdhresrwmkyndiavtksswee 300
Db
    636 LVRDSFGGYRNASAYCLMYINDKAQFLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQR 695
QУ
        301 lvrdsfggyrnasayclmyindkaqfliqeefnketgqplvgietlppdlrdfveednqr 360
Qy
    696 FEKELEEWDAQLAQKALQEKLLASQKLRESETSVTTAQAAGDPEYLEQPSRSDFSKHLKE 755
        361 fekeleewdaqlaqkalqekllasqklresetsvttaqaagdpeyleqpsrsdfskhlke 420
Db
    756 ETIQIITKASHEHEDKSPETVLQSAIKLEYARLVKLAQEDTPPETDYRLHHVVVYFIQNQ 815
Qу
        421 etiqiitkashehedkspetvlqsaikleyarlvklaqedtppetdyrlhhvvvyfiqnq 480
Db
    816 APKKIIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEEVNLEEYEEWHQDYRKFR 875
Qу
        Db
     481 apkkiiektlleqfgdrnlsfderchnimkvaqaklemikpeevnleeyeewhqdyrkfr 540
    876 ETTMYLIIGLENFQRESYIDSLLFLICAYQNNKELLSKGLYRGHDEELISHYRRECLLIL 935
Qу
        541 ettmyliiglenfqresyidsllflicayqnnkellskglyrghdeelishyrrecll-- 598
Db
    936 NLKRKQKPILFFFLHCIKKLNEQAAELFESGEDREVNNGLIIMNEFIVPFLPLLLVDEME 995
Qу
                     599 -----klneqaaelfesgedrevnngliimnefivpflplllvdeme 640
Db
    996 EKDILAVEDMRNRWCSYLGQEMEPHLQEKLTDFLPKLLDCSMEIKSFHEPPKLPSYSTHE 1055
Qy
        641 ekdilavedmrnrwcsylgqemephlqekltdflpklldcsmeiksfheppklpsysthe 700
Db
    1056 LCERFARIMLSLSRTPADGR 1075
Qу
        111111111111111111111
     701 lcerfarimlslsrtpadgr 720
Db
RESULT 10
AAR36730
ID
    AAR36730 standard; Protein; 1264 AA.
XX
AC
    AAR36730;
XX
DT
    26-AUG-1993 (first entry)
xx
    Ubiquitin-specific protease, UBP2.
DE
XX
    Fusion protein; ubiquitin-methionine-beta-galactosidase; UBP2; UBP3;
KW
    expression vector; ubiquitin-specific; protease; UBP1; in vitro;
KW
    transformation; Ub-met-beta-Gal; in vivo.
KW
XX
os
    Synthetic.
XX
    W09309235-A.
```

PN

```
xx
PD
    13-MAY-1993.
XX
                 92WO-US09562.
PF
    06-NOV-1992;
XX
    08-NOV-1991; 91US-0789915.
XX
    (MASI ) MASSACHUSETTS INST TECHNOLOGY.
PΑ
XX
    Baker RT, Tobias JW, Varshavsky A;
ΡI
XX
    WPI; 1993-167700/20.
DR
    N-PSDB; AAQ41289.
DR
хx
    Ubiquitin-specific protease(s) - specifically cleave fusion
PT
    proteins regardless of size, at C-terminus of ubiquitin portion
PT
XX
    Claim 6; Page 47-54; 78pp; English.
PS
XX
    The sequences given in AAR36729-31 represent the ubiquitin-specific
CC
    proteases UBP1, UBP2, and UBP3. These proteases specifically cleave
CC
    the 120 kD fusion protein ubiquitin-methionine-beta-galactosidase
CC
    (Ub-met-beta-Gal) (see also AAR36728). The proteases UBP1 and UBP2
CC
    demonstrate activity both in vivo and in vitro, whereas UBP3 is only
CC
    active in vivo. These proteases have been shown to specifically
    cleave Ub-met-beta-Gal at the C-terminus of the ubiquitin moiety.
CC
    The proteases can be used to deubiquinate fusion proteins in vivo,
CC
    therefore prokaryotic cells having an expression vector one of these
CC
    proteases can be further transformed with an expression vector
CC
    encoding a ubiquitin fusion protein. Such cells will then produce
    a deubiquinated product having a predetermined N-terminal amino acid
CC
CC
    residue.
XX
    Sequence 1264 AA;
SQ
  Query Match 5.7%; Score 318.5; DB 14; Length 1264; Best Local Similarity 19.6%; Pred. No. 1.8e-15;
 Matches 170; Conservative 121; Mismatches 240; Indels 337; Gaps
       4 EQNVLQQSAAQKHQQTF-----LNQLREITGIN----DTQILQQALKDSNGNLELAV 51
Qу
         502 kqdiigqealenallmfkinpkecniselneatllsiykyetsnksqvtsnhltnlknal 561
Db
      52 AFLTAKNAKTPQOEETTYYQTALPGNDRYISVGSQADTNVIDLTGDD------98
Qу
             562 rll----akytksdklkfyvdhep----yralsqaydtlsidesvdediiktaysvkind 613
DЪ
      99 ----KDDLQR---TIALS----- 120
Qу
     | | | | |
Db
     121 -----GITDEEQAI---SRVLEASIAENKACL-----KRTPTEVWRDSRNPY 159
Qу
               674 kgkwfdenvyepdqflilraaltkisiernstlitnflltgtidpnslppenw----- 726
Db
     160 DRKRQDKAPVGLKNVGNTCWFSAVIQSLFNLLEFRRLVLNY-KPPSNAQD------ 208
Qу
                | |: |:||||: ::::| |:: || || | | | |
     727 -----ptginnigntcylnsllqyyfsiaplrryvleyqktvenfndhlsnsghirr 778
     209 ----LPRNQKEHRNLPFMRELRYLFALLVGTKRKYVDPSRAV----- 246
Qy
             : | : | | :: |: : | | | : | | : : | | | : :
     779 iggrqisrgeve-rsiqfiyqlrnlfyamvhtrercvtpskelaylafapsnvevefeve 837
Db
     247 ------EILKDAF---
                                                  ----KSNDSQQQD 262
Qу
                      | |:|
     838 gnkyvdqtqvlsdskkettddafttkikdtslidlemedglngdvgtdanrkknesndae 897
Db
     263 VSE-----FTHKLLDWLEDAFQMKAEEET------DEEK 290
Qу
                                                11:
                          | | | | | | | | | | | |
     898 vsenedttgltsptrvakissdqlenalemgrqqdvtecignvlfqiesgsepirydedn 957
Db
```

```
291 PKNPMV-ELFYG------RFLAVGVLEGKKFENTEMFGQYPLQVNG 329
Qy
         Db
     958 eqydlvkqlfygttkqsivplsatnkvrtkverflslli-----nigdhp---- 1002
     330 FKDLHECLEAAMIEGEIESLHSENSGKSGQEHWFTGLPPVLTFXLSRFEFNQALGRPEKI 389
Qу
         1003 -kdiydafdsyfkd---eyltmeeygdvirtvavttfptilqvqiqrvyydrerlmpfks 1058
Db
     390 HNKLEFPQVLYLDRYMHRNREITRIKREEIKRLKDYLTVLQQRLERYLSY-GSGPKRFPL 448
Qy
           1059 ieplpfkeviymdryadtenplllakkketeemkqklkvmknrqrellsrddsgltr--- 1115
Db
     449 VDVLQYALEFASSKPVCTSPVDDIDASSPPSGSIPSQTLPSTTEQQGALSSELPSTSPSS 508
Qу
            ::: | : : |: |: |
                                                  1116 kdaflesikllesdtikktpl-kiea-----andviktlrnn 1151
Db
     509 VAAISSRSVIHKPFTQSRIPPDLPMHPAPRHITEEELSVLESCLHRWRTEIENDTRDLQE 568
Qу
        : || :: || |:|
    1152 vqni----mklyndinslee 1171
Db
     569 SISRIHRTIELMYSDKSMIQVPYRLHAVLVHEGQANAGHYWAYIFD-HRESRWMKYNDIA 627
Qу
         Db
    1172 kish-----qfdd--fkeygyslfsvfihrgeasyrhywiyikdrnrngiwrkyndet 1222
Qу
     628 VTKSSWEELVRDSFGGYRNASAYCLMYI 655
         ::: ||: :| |:|:
    1223 isevqeeevf--nfnegntatpyflvyv 1248
Db
Result
              Query
  No. Score Match Length DB ID
                                                   Description
  5.9 1264 1 US-07-789-915A-6
5.9 1264 1 US-08-005-002C-6
        327.5
                                                   Sequence 6, Appli
        327.5
                                                   Sequence 6, Appli
              5.9 1264 1 US-08-487-203A-6
4.0 2547 3 US-09-058-489-35
3.8 2555 3 US-09-058-489-36
    3
        327.5
                                                   Sequence 6, Appli
         224
                                                   Sequence 35, Appl
         210
    5
                                                   Sequence 36, Appl
        191.5
                   1786 4 US-08-973-462-8
               3.4
                                                   Sequence 8, Appli
                   1164 4 US-08-923-992A-10
    7
        174.5
               3.1
                                                    Sequence 10, Appl
                   1312 2 US-08-687-080-51
3248 1 US-08-353-700-1
    8
         172
               3.1
                                                    Sequence 51, Appl
        171.5
               3.1
                                                   Sequence 1, Appli
   10
        171.5
               3.1 3248 5 PCT-US95-16216-1
                                                    Sequence 1, Appli
                    1312 2 US-08-592-126-148
                                                    Sequence 148, App
Result
             Ouerv
       Score Match Length DB ID
  No.
                                                   Description
             8.7 1302 2 T23236
    1 485.5
                                                   hypothetical prote
                   1272 2 S60999
1108 2 T41188
        323.5
               5.8
                                                   ubiquitin-specific
       316.5
    3
               5.7
                                                   probable ubiquitin
                   1221 2 T30529
    4
         310
               5.6
                                                  ubiquitin carboxyl
    5
         287
                    1130 2 T23104
1133 2 T23103
               5.1
                                                  hypothetical prote
    6
         287
               5.1
                                                  hypothetical prote
                    1230 2 T19899
       266.5
               4.8
                                                  hypothetical prote
    8
        263
                    3187 2 JC5837
               4.7
                                                  364K Golgi complex
                    1230 2 $53974
        253.5
               4.5
                                                  hypothetical prote
RESULT
hypothetical protein K02C4.3 - Caenorhabditis elegans
C; Species: Caenorhabditis elegans
C;Date: 15-Oct-1999 #sequence_revision 15-Oct-1999 #text change 15-Oct-1999
C; Accession: T23236
R; Lightning, J.
submitted to the EMBL Data Library, January 1995
A; Reference number: Z19713
A; Accession: T23236
A; Status: preliminary; translated from GB/EMBL/DDBJ
```

```
A; Molecule type: DNA
A; Residues: 1-1302 <WIL>
A;Cross-references: EMBL:Z47811; PIDN:CAA87786.1; GSPDB:GN00020; CESP:K02C4.3
A; Experimental source: clone K02C4
C;Genetics:
A; Gene: CESP: K02C4.3
A; Map position: 2
A; Introns: 10/1; 31/3; 84/3; 279/3; 464/1; 745/1; 957/2; 978/3; 1090/2; 1201/3; 1270/3
 Query Match 8.7%; Score 485.5; DB 2; Length 1302; Best Local Similarity 23.2%; Pred. No. 1.2e-18;
 Matches 237; Conservative 139; Mismatches 353; Indels 293; Gaps
     90 NVIDLTGDDKDDLQRTIALSLAESNRAFRETGITDEEQAISRVLEASIAENKACLKRTPT 149
Οy
       150 NISEISKKEEVEMQSAIQQSLASS------ASQNISR------PT 182
Dh
    150 EVWRDSRNPYDRKRQDKAPVGLKNVGNTCWFSAVIQSLFNLLEFRRLVLNYKPPSNAQDL 209
Qу
            183 ML---MSNLEDMVRNPNFSTGLYNSGNTCWLNCLSQVLYSIPKFRSILYHCAPLSWHEQP 239
Db
    210 PRNOK----EHRNLPFMRELRYLFALLVGTKRKYVDPSRAVEILKDAFKSND-----SQQ 260
Ov
         Db
    240 ITNVKIENQQHAELLML--FRGLFAELQFSEMKYIEVGPLINMVDKLSKSSKGPSTIGTQ 297
    261 QDVSEFTHKLLDWLEDAF----- QMKAE--EETDEEK------ 290
Qy
Db
    298 QDATEMLTLIFDWLQRAFDAALHAQLNPEFSNVSDEENLVISDSTTTAPNSDIIGAPPGY 357
    Qу
                  358 NAANLSLPSSSHVDPKSTLNPMYVNEKEPSSTPTSLFGTRSKTIEVNESMDTEAATSSNL 417
Db
    310 EGKKFEN---
               -----TEMFGQ----- 322
Qy
                                     || :
    418 PGNSVENHPNPAAPEVDDNKKAFCDKLKESFNNIFSSVCYTESVAEDGTVSVKSNVRNCP 477
    323 --YPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQEHWFTGLPPVLTFXLSRFEFN 380
Οv
         478 QFFQLQVT-YGNLHDALEAATFD-----HGLGNTASHVRNLYDPLPAVIFFGLSRFSFN 530
Db
    381 QALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIKRLKDYLTVLQQRLERYLSYG 440
Qу
         : |:|:| ||:::::|||: |:| | : :| |::::|
    531 SNI--ESKLHDKFTFPKIIFMDRYLKCNKEQLVQLRSHRELCRDSLSEVRAKLSGLRRYP 588
Db
    441 SGPKRFPLVDVLQYALEFASS-KPVCTSPVDDIDASSPPSGSIPSQTLPS---TTEQQGA 496
Qу
            589 QGNGEVRLEDSFQTVWQAVSNFREFVTFYL------KVSQKTFFSREDAHENTAF 637
Db
    497 LSSELPSTSPSSVAAISSRSV-----IHKPFTQSRIPPDLPMHPAPRHITEEELSVLESC 551
Qy
       Dh
    638 VGPLTPSTYQSSSDNCSSKFVKDGGKLFPTFTEGFFPGKAAF-----IETLQNM 686
    552 LHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHEGQANAGHYWAY 611
Qу
       687 LEALKTE----ERDCLAEEARLQEVIDQTYEVPELQQHKYELHAIIVHSGEANRGHYWTY 742
Db
Οv
    612 ----IFDHRESRWMKYNDIAVTKSSWEELVRDSFG-GYRNA-SAYCLMYINDKAOFLIOE 665
            743 KLKKSIDGLE-EWEKLNDQNADRVDWPKVESDSFGTGSRDAPSAYMLMYVRSDAEWLVSA 801
Db
    666 EFNKETGQPLVGIETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALQEKLLASQKLRES 725
Qу
       802 D--KLTA--LEAFETIPPDLQEKVLQKRDEFKEKL-----QRFRENKEFNYQQFSVD 849
Db
    726 ETSVTTAQAAGDPEYLEQPSRSDFSKHLKE-ETIQIITKASHEHEDKSPETVLQSAIKLE 784
Qу
         850 SPTVQSTE-----ETP--SSFSWYRDELEDIDI-----GDENANP-----TKND 886
Db
    785 YARLVKLAQEDTP--PETDYRLHHVVVYFIQNQ----APKKIIE-----KTLLE-- 827
Qу
```

```
887 YLLNARLDSYSVPIAPDVETSEMKRMVSQMWNQITKIAPRKYTDSQDLLDSNLRSVMEGE 946
Db
     828 ----QFGDRNLSFDERCHNIMKVAQAKLEMIKPEEVNLEEYEEWHQDYRKFRETTMYLII 883
Qy
             947 SGGINFINSRLGYD--IHELRSDADNDVEGVYNAFIN--EYLGLVKDLHELQNSKFVVFV 1002
Db
     884 GLENFQRESYIDSLLFLICAYQNNKEL------LSKGLYRGHDEE-----LIS 925
Qу
         1: || :: |:|: ||
                                       - 11
                                                    ||:
    1003 GFQ-LQR-IHVPVLRYLLVRAMAVSELGIISQRANNELSGMSSNSHDKGTAMLQIALLLS 1060
Db
     926 HY 927
Qу
Db
    1061 HF 1062
Result
               Ouery
        Score Match Length DB ID
                                                        Description
  No.
       -----
                      1087 1 UBPP_HUMAN
    1
       5410
                96.9
                                                        Q9uhp3 homo sapien
                      1055 1 UBPP_MOUSE
1302 1 UBPY_CAEEL
        5091
                91.2
                                                         P57080 mus musculu
    2
                                                        009931 caenorhabdi
    3
        485.5
                8.7
                      1272 1 UBP2 YEAST
                                                        Q01476 saccharomyc
        323.5
                 5.8
                      1108 1 UBPB_SCHPO
1221 1 UBP2_KLULA
                                                        Q09879 schizosacch
    5
        316.5
                5.7
    6
          310
                 5.6
                                                        042726 kluyveromyc
                       898 1 UBPE DROME
                                                        Q24574 drosophila
        287.5
                5.2
    7
                                                        Q93009 homo sapien
                      1102 1 UBP7_HUMAN
    8
          276
                 4.9
                       1230 1 UBPF_YEAST
499 1 UBPH_YEAST
                      1230 1
                                                        P50101 saccharomyc
    9
        253.5
                 4.5
                                                        P43593 saccharomyc
   10
          226
                4.0
   11
          224
                 4.0
                      2547 1
                               FAFX_HUMAN
                                                        Q93008 h probable
RESULT 1
UBPP HUMAN
    UBPP HUMAN
                   STANDARD;
                                 PRT; 1087 AA.
ID
AC
    O9UHP3:
    30-MAY-2000 (Rel. 39, Created)
    01-OCT-2000 (Rel. 40, Last sequence update)
DT
DT
    01-OCT-2000 (Rel. 40, Last annotation update)
    UBIQUITIN CARBOXYL-TERMINAL HYDROLASE 25 (EC 3.1.2.15) (UBIQUITIN
DE
    THIOLESTERASE 25) (UBIQUITIN-SPECIFIC PROCESSING PROTEASE 25)
DE
     (DEUBIQUITINATING ENZYME 25) (USP ON CHROMOSOME 21).
DE
    USP25 OR USP21.
GN
os
    Homo sapiens (Human).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OC
OX
    NCBI_TaxID=9606;
RN
    [1]
    SEQUENCE FROM N.A. (SHORT AND LONG ISOFORMS).
RP
RC
    TISSUE=Fetal brain:
RX
    MEDLINE=20112753; PubMed=10644437;
RA
    Valero R., Marfany G., Gonzalez-Angulo O., Gonzalez-Gonzalez G.,
RA
    Puelles L., Gonzalez-Duarte R.;
     "USP25, a novel gene encoding a deubiquitinating enzyme, is located in
    the gene-poor region 21q11.2.";
RT
RL
    Genomics 62:395-405(1999).
RN
    SEQUENCE FROM N.A. (SHORT ISOFORM).
RP
    MEDLINE=20080730; PubMed=10612803;
RX
    Groet J., Ives J.H., Jones T.A., Danton M., Flomen R.H., Sheer D.,
RA
    Hrascan R., Pavelic K., Nizetic D.;
     "Narrowing of the region of allelic loss in 21q11-21 in squamous non-
RT
RT
    small cell lung carcinoma and cloning of a novel ubiquitin-specific
RТ
    protease gene from the deleted segment.";
    Genes Chromosomes Cancer 27:153-161(2000).
RL
     -!- FUNCTION: INVOLVED IN THE UBIQUITIN-DEPENDENT PROTEOLYTIC PATHWAY
CC
CC
        IN CONJUNCTION WITH THE 26S PROTEASOME (BY SIMILARITY).
    -!- CATALYTIC ACTIVITY: UBIQUITIN C-TERMINAL THIOLESTER + H(2)O =
CC
CC
        UBIQUITIN + A THIOL.
```

-! - ALTERNATIVE PRODUCTS: 2 ISOFORMS; A LONG FORM (SHOWN HERE) AND A

SHORT FORM; ARE PRODUCED BY ALTERNATIVE SPLICING.

CC

```
-!- TISSUE SPECIFICITY: FOUND IN MOST ADULT AND FETAL TISSUES;
CC
       EXPRESSION IS MODERATELY HIGH IN TESTIS, PANCREAS, KIDNEY,
CC
       SKELETAL MUSCLE, LIVER, LUNG, PLACENTA, BRAIN, HEART, BUT VERY LOW
CC
       IN PERIPHERAL BLOOD, COLON, SMALL INTESTINE, OVARY, PROSTATE,
CC
       THYMUS AND SPLEEN.
CC
    -!- SIMILARITY: BELONGS TO PEPTIDASE FAMILY C19; ALSO KNOWN AS
CC
       FAMILY 2 OF UBIQUITIN CARBOXYL-TERMINAL HYDROLASES.
CC
CC
    This SWISS-PROT entry is copyright. It is produced through a collaboration
CC
    between the Swiss Institute of Bioinformatics and the EMBL outstation
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    the European Bioinformatics Institute. There are no restrictions on its
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    use by non-profit institutions as long as its content is in no way
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    modified and this statement is not removed. Usage by and for commercial
CC
    entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC
    or send an email to license@isb-sib.ch).
CC
CC
    EMBL; AF170562; AAF32263.1; -.
DR
    EMBL; AF134213; AAF24998.1; -.
DR
DR
    MIM; 604736; -
    InterPro; IPR001394; -.
DR
DR
    Pfam; PF00442; UCH-1; 1.
    Pfam; PF00443; UCH-2; 1.
DR
    PROSITE; PS00972; UCH_2_1; 1.
DR
    PROSITE; PS00973; UCH 2 2; 1.
DR
    PROSITE; PS50235; UCH_2_3; 1.
DR
    Ubiquitin conjugation; Hydrolase; Thiol protease; Multigene family;
KW
    Alternative splicing.
KW
                             BY SIMILARITY.
                    178
    ACT SITE
              178
    ACT SITE
              599
                    599
                             BY SIMILARITY.
FT
                             BY SIMILARITY.
                    607
              607
FT
    ACT_SITE
                             MISSING (IN SHORT ISOFORM).
              780
                    811
FT
    VARSPLIC
              544
                    544
                             K \rightarrow E (IN REF. 2).
FT
    CONFLICT
    SEQUENCE 1087 AA; 125748 MW; 0699DDB7451B2C6C CRC64;
                      96.9%; Score 5410; DB 1; Length 1087;
  Ouerv Match
  Best Local Similarity 94.9%; Pred. No. 1.5e-283;
                                            3; Indels
                           1; Mismatches
  Matches 1051; Conservative
       1 MTVEQNVLQQSAAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTAKNAK 60
         1 MTVEQNVLQQSAAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTAKNAK 60
Db
      61 TPQQEETTYYQTALPGNDRYISVGSQADTNVIDLTGDDKDDLQRTIALSLAESNRAFRET 120
Qу
         61 TPQQEETTYYQTALPGNDRYISVGSQADTNVIDLTGDDKDDLQRAIALSLAESNRAFRET 120
Db
     121 GITDEEQAISRVLEASIAENKACLKRTPTEVWRDSRNPYDRKRQDKAPVGLKNVGNTCWF 180
Qy
         121 GITDEEQAISRVLEASIAENKACLKRTPTEVWRDSRNPYDRKRQDKAPVGLKNVGNTCWF 180
     181 SAVIQSLFNLLEFRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV 240
Qу
         181 SAVIQSLFNLLEFRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV 240
Db
     241 DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEEETDEEKPKNPMVELFY 300
Qу
         241 DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEEETDEEKPKNPMVELFY 300
Db
      301 GRFLAVGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQE 360
Οv
         301 GRFLAVGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQE 360
      361 HWFTGLPPVLTFXLSRFEFNQALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIK 420
Qу
         361 HWFTELPPVLTFELSRFEFNQALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIK 420
Db
      421 RLKDYLTVLOORLERYLSYGSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSPPSG 480
Qу
         421 RLKDYLTVLQQRLERYLSYGSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSPPSG 480
Db
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481 SIPSQTLPSTTEQQGALSSELPSTSPSSVAAISSRSVIHKPFTQSRIPPDLPMHPAPRHI 540
Qу
         Db
     481 SIPSOTLPSTTEOOGALSSELPSTSPSSVAAISSRSVIHKPFTOSRIPPDLPMHPAPRHI 540
Qу
     541 TEEELSVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHE 600
         Db
     541 TEEKLSVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHE 600
     601 GQANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKAQ 660
Qу
         Db
     601 GOANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKAO 660
     661 FLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALQEKLLASQ 720
Qу
         661 FLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALQEKLLASQ 720
Db
     721 KLRESETSVTTAQAAGDPEYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLOS- 779
Qу
         Db
     721 KLRESETSVTTAQAAGDPEYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQSI 780
                                   -AIKLEYARLVKLAQEDTPPETDYRLHHVV 808
Qу
                                   111111111111111111111111111111111111
     781 MMTPNMQGIIMAIGKSRSVYDRCGPEAGFFKAIKLEYARLVKLAQEDTPPETDYRLHHVV 840
Dh
     809 VYFIQNQAPKKIIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEEVNLEEYEEWH 868
Qу
         Db
     841 VYFIQNQAPKKIIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEEVNLEEYEEWH 900
     869 QDYRKFRETTMYLIIGLENFQRESYIDSLLFLICAYQNNKELLSKGLYRGHDEELISHYR 928
Qу
         Db
     901 QDYRKFRETTMYLIIGLENFQRESYIDSLLFLICAYQNNKELLSKGLYRGHDEELISHYR 960
Qy
     929 RECLLILNLKRKQKPILFFFLHCIKKLNEQAAELFESGEDREVNNGLIIMNEFIVPFLPL 988
                              961 RECLL-----
Db
                             -KLNEQAAELFESGEDREVNNGLIIMNEFIVPFLPL 1000
     989 LLVDEMEEKDILAVEDMRNRWCSYLGQEMEPHLQEKLTDFLPKLLDCSMEIKSFHEPPKL 1048
Qу
         1001 LLVDEMEEKDILAVEDMRNRWCSYLGQEMEPHLQEKLTDFLPKLLDCSMEIKSFHEPPKL 1060
Db
    1049 PSYSTHELCERFARIMLSLSRTPADGR 1075
Οv
         Db
    1061 PSYSTHELCERFARIMLSLSRTPADGR 1087
RESULT
UBPP_MOUSE
ID
    UBPP MOUSE
                 STANDARD;
                              PRT; 1055 AA.
    P57080:
AC
DT
    01-OCT-2000 (Rel. 40, Created)
DT
    01-OCT-2000 (Rel. 40, Last sequence update)
    01-OCT-2000 (Rel. 40, Last annotation update)
DT
    UBIQUITIN CARBOXYL-TERMINAL HYDROLASE 25 (EC 3.1.2.15) (UBIQUITIN
DE
    THIOLESTERASE 25) (UBIQUITIN-SPECIFIC PROCESSING PROTEASE 25)
DE
    (DEUBIQUITINATING ENZYME 25) (MUSP25).
GN
    USP25.
os
    Mus musculus (Mouse).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OC
OC
ox
    NCBI_TaxID=10090;
RN
    [1]
    SEQUENCE FROM N.A.
RP
RC
    TISSUE=Kidney;
    MEDLINE=20112753; PubMed=10644437;
RX
    Valero R., Marfany G., Gonzalez-Angulo O., Gonzalez-Gonzalez G.,
RA
    Puelles L., Gonzalez-Duarte R.;
RA
RT
    "USP25, a novel gene encoding a deubiquitinating enzyme, is located in
    the gene-poor region 21q11.2.";
RТ
RL
    Genomics 62:395-405(1999).
    -!- FUNCTION: INVOLVED IN THE UBIQUITIN-DEPENDENT PROTEOLYTIC PATHWAY
CC
CC
       IN CONJUNCTION WITH THE 26S PROTEASOME (BY SIMILARITY).
```

```
-!- CATALYTIC ACTIVITY: UBIQUITIN C-TERMINAL THIOLESTER + H(2)O =
       UBIQUITIN + A THIOL.
    -!- TISSUE SPECIFICITY: HIGHLY EXPRESSED IN TESTIS. ALSO FOUND IN
CC
       BRAIN, SKELETAL MUSCLE, LIVER AND HEART.
CC
    -!- SIMILARITY: BELONGS TO PEPTIDASE FAMILY C19; ALSO KNOWN AS
       FAMILY 2 OF UBIQUITIN CARBOXYL-TERMINAL HYDROLASES.
CC
   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC
   between the Swiss Institute of Bioinformatics and the EMBL outstation -
   the European Bioinformatics Institute. There are no restrictions on its
CC
   use by non-profit institutions as long as its content is in no way
CC
   modified and this statement is not removed. Usage by and for commercial
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    entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC
    or send an email to license@isb-sib.ch).
CC
CC
   EMBL; AF170563; AAF32264.1; -.
   MGD; MGI:1353655; Usp25.
DR
DR
    PROSITE; PS00972; UCH_2_1; 1.
    PROSITE; PS00973; UCH_2_2; 1.
    PROSITE; PS50235; UCH 2 3; 1.
DR
KW
   Ubiquitin conjugation; Hydrolase; Thiol protease; Multigene family.
   ACT SITE
             178 178
                           BY SIMILARITY.
FT
                 600
           600
FT
   ACT_SITE
                           BY SIMILARITY.
             608
                  608
                           BY SIMILARITY.
FT
    ACT SITE
   SEQUENCE 1055 AA; 121426 MW; CDFDFD1052745D70 CRC64;
                     91.2%; Score 5091; DB 1; Length 1055;
 Query Match
 Best Local Similarity 91.5%; Pred. No. 2.1e-266;
 Matches 985; Conservative 29; Mismatches 40; Indels
                                                    22: Gaps
                                                              3:
      1 MTVEQNVLQQSAAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTAKNAK 60
Qу
        1 MTVEQNVLQQSAAQKHQQTFLNQLREITGINDAQILQQALKDSNGNLELAVAFLTAKNAK 60
Db
     61 TPQQEETTYYQTALPGNDRYISVGSQADTNVIDLTGDDKDDLQRTIALSLAESNRAFRET 120
Ov
        Db
     61 TPPQEETGYYQTALPGNDRYISVGSQADANVIDLTGDDKDDLQRAIALSLAESNRAFRET 120
    121 GITDEEQAISRVLEASIAENKACLKRTPTEVWRDSRNPYDRKRQDKAPVGLKNVGNTCWF 180
Qy
        121 GITDEEQAISRVLEASIAENKACLKRTPIEVWRDSRNPYDRKRQEKAPVGLKNVGNTCWF 180
Db
    181 SAVIQSLFNLLEFRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV 240
Qу
        181 SAVIQSLFNLLEFRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV 240
Db
    241 DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEEETDEEKPKNPMVELFY 300
Qy
        Db
     241 DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEEETDEEKPKNPMVELFY 300
    301 GRFLAVGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQE 360
Qу
        301 GRFLAMGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSDNSGKSGQE 360
Db
    361 HWFTGLPPVLTFXLSRFEFNQALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIK 420
Qу
        Db
    361 HWFTELPPVLTFELSRFEFNOALGRPEKIHNKLKFPOVLYLDRYMHRNREITRIKREEIK 420
     421 RLKDYLTVLOORLERYLSYGSGPKRFPLVDVLOYALEFASSKPVCTSPVDDIDASSPPSG 480
Ov
        Db
     421 RLKDYLTVLQQRLERYLSYGSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSSASG 480
    481 SIPSQTLPSTTEQQGALSSELP-STSPSSVAAISSRSVIHKPFTQSRIPPDLPMHPAPRH 539
Qy
    Db
    540 ITEEELSVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVH 599
Qy
        541 ITEEELCVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVH 600
```

```
600 EGQANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKA 659
Qу
       601 EGOANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYIDDKA 660
Db
Qу
    660 QFLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALOEKLLAS 719
        661 QFLIQEEFNKETGQALVGMETLLPDLRDFVEEDNQRFEKELEEWDTQLAQRSLQEKLLAA 720
Db
Qу
    720 QKLRESETSVTTAQAAGDPEYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQS 779
        1411:1 | 11111 | :11141111 | 1411:::| 1111: 141 | 1411
Db
    721 PKLREAEASATTAQAGG-ADYLEQPSRSDLSKHWKEETLRVIAKASHDLEDKGPETVLOS 779
    780 AIKLEYARLVKLAQEDTPPETDYRLHHVVVYFIQNQAPKKIIEKTLLEQFGDRNLSFDER 839
Qу
       780 AIKLEYSRLVKLAQEDTPPETDYRLHHVLVYFIQNQAPKKIIEKTLLEQFGDRNLSFDER 839
Db
    840 CHNIMKVAQAKLEMIKPEEVNLEEYEEWHQDYRKFRETTMYLIIGLENFQRESYIDSLLF 899
Qу
        Db
    840 CLNIMKVAQAKLEMIKPEEVNLEEYEEWHADYKKFRETTMYLITGLENFQRESYIDSLLF 899
Qу
    900 LICAYQNNKELLSKGLYRGHDEELISHYRRECLLILNLKRKQKPILFFFLHCIKKLNEQA 959
       900 LLCAYQNNKELLSKGPYRGHDGELISHYRRECLL------KLNEQA 939
Db
    960 AELFESGEDREVNNGLIIMNEFIVPFLPLLLVDEMEEKDILAVEDMRNRWCSYLGQEMEP 1019
Qy
       940 AELFESGEDGDVNNGLIIMNEFIVPFLPLLLVDDMEEKDILAVEDMRNRWCSYLGQEMEA 999
Dh
   1020 HLQEKLTDFLPKLLDCSMEIKSFHEPPKLPSYSTHELCERFARIMLSLSRTPADGR 1075
Qу
       1000 NLQEKLTDFLPKLLDCSTEIKGFHEPPKLPSYSAHELCERFARIMLSLSRTPADGR 1055
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Result No.	Score	Query Match	Length	DB	ID	Description
1	3816	68.4	737	4	Q9H9W1	Q9h9w1 homo sapien
2	2721	48.8	523	4	Q9HA22	Q9ha22 homo sapien
3	1875	33.6	757	4	Q9P213	Q9p213 homo sapien
4	303	5.4	1124	10	Q9SF08	Q9sf08 arabidopsis
5	297.5	5.3	1116	10	Q9FPT1	Q9fpt1 arabidopsis
6	297	5.3	1126	10	Q9FG10	Q9fg10 arabidopsis
7	296	5.3	1248	5	Q9VRP1	Q9vrp1 drosophila
8	288.5	5.2	599	10	Q9FU99	Q9fu99 arabidopsis
9	287	5.1	1130	5	045624	045624 caenorhabdi
10	287	5.1	1133	5	045623	045623 caenorhabdi
11	283.5	5.1	1141	3	Q9P3U0	Q9p3u0 schizosacch
4 5 6 7 8 9	303 297.5 297 296 288.5 287 287	5.4 5.3 5.3 5.3 5.2 5.1	1124 1116 1126 1248 599 1130 1133	10 10 10 5 10 5	Q9SF08 Q9FPT1 Q9FG10 Q9VRP1 Q9FU99 O45624 O45623	Q9sf08 arabidopsis Q9fpt1 arabidopsis Q9fg10 arabidopsis Q9vrp1 drosophila Q9fu99 arabidopsis O45624 caenorhabdi O45623 caenorhabdi

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RESULT
O9H9W1
     Q9H9W1
                  PRELIMINARY;
                                     PRT:
                                             737 AA.
     Q9H9W1;
AC
     01-MAR-2001 (TrEMBLrel. 16, Created)
01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT
DT
     01-MAR-2001 (TrEMBLrel. 16, Last annotation update)
     CDNA FLJ12512 FIS, CLONE NT2RM2001730, WEAKLY SIMILAR TO PROBABLE
     UBIQUITIN CARBOXYL-TERMINAL HYDROLASE K02C4.3 (EC 3.1.2.15).
     Homo sapiens (Human).
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
OC
     Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX
     NCBI TaxID≃9606;
RN
     [1]
RP
     SEQUENCE FROM N.A.
     Isogai T., Ota T., Hayashi K., Sugiyama T., Otsuki T., Suzuki Y.,
RA
RΑ
     Nishikawa T., Nagai K., Sugano S., Aotsuka S., Yoshikawa Y.,
     Matsunawa H., Ishii S., Kawai Y., Saito K., Yamamoto J., Wakamatsu A.,
RA
     Nakamura Y., Nagahari K., Masuho Y., Sasaki N.;
RT
     "NEDO human cDNA sequencing project.";
     Submitted (AUG-2000) to the EMBL/GenBank/DDBJ databases.
```

DR EMBL; AK022574; BAB14107.1; -. SQ SEQUENCE 737 AA; 85842 MW; D660BB2A18077E10 CRC64;

Bes		atch 68.4%; Score 3816; DB 4; Length 737; cal Similarity 97.1%; Pred. No. 6.4e-221; 735; Conservative 0; Mismatches 2; Indels 20; Gaps 1;
Qу	319	MFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQEHWFTGLPPVLTFXLSRFE 378
Db	1	MFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQEHWFTELPPVLTFELSRFE 60
Qу	379	FNQALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIKRLKDYLTVLQQRLERYLS 438
Db	61	FNQALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIKRLKDYLTVLQQRLERYLS 120
Qу	439	YGSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSPPSGSIPSQTLPSTTEQQGALS 498
Db	121	YGSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSPPSGSIPSQTLPSTTEQQGALS 180
Qу	499	SELPSTSPSSVAAISSRSVIHKPFTQSRIPPDLPMHPAPRHITEEELSVLESCLHRWRTE 558
Db	181	SELPSTSPSSVAAISSRSVIHKPFTQSRIPPDLPMHPAPRHITEEELSVLESCLHRWRTE 240
Qу	559	IENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHEGQANAGHYWAYIFDHRES 618
Db	241	IENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHEGQANAGHYWAYIFDHRES 300
Qу		RWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKAQFLIQEEFNKETGQPLVGI 678
Db	301	RWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKAQFLIQEEFNKETGQPLVGI 360
Qу	679	ETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALQEKLLASQKLRESETSVTTAQAAGDP 738
Db	361	ETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALQEKLLASQKLRESETSVTTAQAAGDP 420
Qу		EYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQSAIKLEYARLVKLAQEDTPP 798
Db	421	EYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQSAIKLEYARLVKLAQEDTPP 480
Qу		ETDYRLHHVVVYFIQNQAPKKIIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEE 858
Db		ETDYRLHHVVVYFIQNQAPKKIIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEE 540
Qу		VNLEEYEEWHQDYRKFRETTMYLIIGLENFQRESYIDSLLFLICAYQNNKELLSKGLYRG 918
Db		VNLEEYEEWHQDYRKFRETTMYLIIGLENFQRESYIDSLLFLICAYQNNKELLSKGLYRG 600
QУ		HDEELISHYRRECLLILNLKRKQKPILFFFLHCIKKLNEQAAELFESGEDREVNNGLIIM 978
Db		HDEELISHYRRECLLKLNEQAAELFESGEDREVNNGLIIM 640
Qу		NEFIVPFLPLLLVDEMEEKDILAVEDMRNRWCSYLGQEMEPHLQEKLTDFLPKLLDCSME 1038
Db		NEFIVPFLPLLLVDEMEEKDILAVEDMRNRWCSYLGQEMEPHLQEKLTDFLPKLLDCSME 700
Qy -		IKSFHEPPKLPSYSTHELCERFARIMLSLSRTPADGR
Db	701	IKSFHEPPKLPSYSTHELCERFARIMLSLSRTPADGR 737